PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 042881-0217	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/IB2006/002771	International filing date *(day/month/year)* 27 June 2006 (27.06.2006)	Priority date *(day/month/year)* 28 June 2005 (28.06.2005)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant BIOMIRA, INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 10 January 2008 (10.01.2008)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Cecile Chatel e-mail: pt13.pct@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* 27 February 2007 (27-02-2007)

Applicant's or agent's file reference
042881-0217

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2006/002771	27 June 2006 (27-06-2006)	28 June 2005 (28-06-2005)

International Patent Classification (IPC) or both national classification and IPC
IPC: ***A61K 38/16*** (2006.01) , ***A61K 9/127*** (2006.01) , ***A61P 35/00*** (2006.01)

Applicant
BIOMIRA, INC. ET AL

1. This opinion contains indications relating to the following items :

[X]	Box No. I	Basis of the opinion
[ ]	Box No. II	Priority
[X]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[X]	Box No. VI	Certain documents cited
[X]	Box No. VII	Certain defects in the international application
[X]	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA	Date of completion of this opinion	Authorized officer
Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	23 February 2007 (23-02-2007)	Raffaele Salvino 819- 997-3031

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   [X] the international application in the language in which it was filed

   [ ] a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :

   a. type of material

      [X] a sequence listing

      [ ] table(s) related to the sequence listing

   b. format of material

      [X] on paper

      [X] in electronic form

   c. time of filing/furnishing

      [X] contained in the international application as filed.

      [X] filed together with the international application in electronic form

      [ ] furnished subsequently to this Authority for the purposes of search.

3. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statement that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments :

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of :

[ ] the entire international application

[X] claim Nos. 1-30

because:

[X] the said international application, or the said claim Nos. 1-30 relate to the following subject matter which does not require an international search *(specify)* :

Claims 1-30, directed to a method for treatment of the human or animal body by surgery or therapy which the International Search Authority is not required to establish a written opinion under Rule 67.1(iv) of the PCT. Regardless, this Authority has established a written opinion based on the alleged effects of the product defined in claims 1-30.

[X] the description, claims or drawings *(indicate particular elements below)* or said claim Nos. 1-12, 14-17, 29 and 30 are so unclear that no meaningful opinion could be formed *(specify)* :

The subject matter defined by the term "immunologically active variant" as it relates to the polypeptide sequences of SEQ ID Nos:1 and 2 encompasses polypeptides that are not defined in terms of a distinguishing technical feature as required under Article 6 of the PCT. The description discloses said term includes an unlimited number of amino acid deletions, substitutions and additions to the defined polypeptides reducing the subject matter merely to a product defined by function. Consequently, the written opinion of claims 1-12, 14-17, 29 and 30 has been established based solely on the definition of "immunologically active variant" found on page 13 line 21 to page 14 line 2 i.e. a polypeptide sequence defined as being at least 80% identical to the amino acid sequence selected from the group consisting of SEQ ID NOs:1 and 2.

[ ] the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify):*

[ ] no international search report has been established for said claims Nos.

[ ] a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

[ ] furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

[ ] furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

[ ] pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

[ ] a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

[ ] the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

[ ] See Supplemental Box for further details.

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	29 and 30	YES
	Claims	1-28	NO
Inventive step (IS)	Claims	none	YES
	Claims	1-30	NO
Industrial applicability (IA)	Claims	1-30	YES
	Claims	none	NO

2. Citations and explanations :

The documents referred to below are numbered in order of appearance of the documents cited in the International Search Report:

D1: NORTH N. and BUTTS C., Expert Rev. Vaccines, June 2005, Vol. 4, No. 3, pp. 249-257, ISSN 1744-8395
D2: PALMER M. et al., Clinical Lung Cancer, August 2001, Vol. 3, No. 1, pp. 49-57, ISSN 1525-7304
D5: US20020051813 A1, BONI L. et al. [US], 2 May, 2002
D6: MACLEAN G.D. et al., J. Immunotherapy, June 1997, Vol. 20, No. 1, pp. 70-78, ISSN 1524-9557

The present application is directed to a method of treating an individual with non-small cell lung cancer (NSCLC) or prostate cancer comprising administering a MUC-1 based formulation comprising a liposome having at least one polypeptide with an amino acid sequence selected from the group consisting of the amino acid sequence of SEQ ID NO. 1, 2 and immunologically active variants thereof. SEQ ID NO.1 is a 25 amino acid MUC-1 core repeat sequence whereas SEQ ID No. 2 is a derivatized version thereof (i.e. having two additional amino acids added at the C-terminal end, one being lipidated). The formulation may be a vaccine and includes at least one adjuvant such as lipid A or interleukin-2. Such formulations used in said method provide for a method to improve or maintain the quality of life of said individual.

Novelty and Inventive Step:

D1 and D2 each separately disclosed a method of treating patients with non-small cell lung cancer comprising injecting a BLP25 liposome based vaccine comprising a polypeptide defined by the amino acid sequence of SEQ ID NO: 2. The vaccine further comprises at least one adjuvant (Lipid A) and other additional liposomal lipids. The patients were pre-treated with cyclophosphamide. They were evaluated during the treatment by measuring T cell proliferation. Further, D1 and D2 separately disclosed that the vaccine had the potential to extend the survival of patients with lung cancer, particularly patients with Stage IIIB locoregional NSCLC. In view of D1 or D2, claims 1, 3-5 and 7-17 are not novel and thus do not comply with Article 33(2) of the PCT.

D1 further discloses that the incorporation of IL-2 as an additional adjuvant in their liposomal vaccine provides benefit (see page 251). Also, D1 discloses the method leads to a maintenence of quality of life as measured by established parameters. Last, the vaccine also shows promise for patients with prostate cancer when administered thereto, having the potential to prolong prostate-specific antigen (PSA) doubling times in men with biochemical failure post prostatectomy. Therefore, claims 2, 6, 18, 20, 21, 23-25, 27 and 28 are not novel and therefore fail to comply with Article 33(2) of the PCT in view of D1.

With respect to claims 18 and 19, the examiner considers the subject matter of claims 18 and 19 merely to be a further characterization of the method disclosed in D2 or D1 respectively.. The treatment for NSCLC patients disclosed in D2 and prostate cancer patients in D1 and those disclosed in the present application are the same and thus evaluation of quality of life parameters is merely an obvious extension of the method disclosed in D1 or D2. No inventive step would be required by a person skilled in the art to evaluate known quality of life parameters following the method disclosed in D1 or D2. As such, claims 18 and 19 are non-compliant with Article 33(3) of the PCT in view of D2 or D1 respectively.

(continued on Supplemental Box, see Continuation of Box No. V)

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
WO2005112546 A2	01-12-2005	01-04-2005	04-06-2004

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted :

1. For clarity, the expression "the antigen" found on the last line of page 6 should read "CA27.29.

2. The data qualification defined by the asterisks in Figure 16 are not described therein or anywhere in the description.

3. Reference to Figure 1 on page 52 is not correct based on the contents of Figure 1 and the disclosure referring to the figure on page 52.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

1. Claims 11, 18 and 19 do not comply with Article 6 of the PCT. The term "quality of life" is vague. Although the reader may be able to contemplate examples that fall under such a term, the full scope encompassed by said term is unclear.

2. Claims 11 and 20 do not comply with Article 6 of the PCT. The term "symptoms" as it relates to non-small cell lung cancer or prostate cancer is vague. Although the reader may be able to contemplate examples that fall under such a term, the full scope encompassed by said term is unclear.

3. Claim 11 does not comply with Article 6 of the PCT because of its dependency on claims 9 and 10. The evaluations defined in claim 11 are unrelated to that defined in claims 9 and 10 i.e. evaluating an immune reaction in a treated subject.

4. . Claim 12 does not comply with Article 6 of the PCT because of its dependency on claim 2. The cancer sub-types defined in claim 12 relate to NSCLC and not prostate cancer which is the subject matter of claim 2.

5. Claim 29 does not comply with Article 6 of the PCT because of the word "high" is a relative term that is not put into a clear and specific context.

6. The description does not comply with Article 5 of the PCT. The statements found on page 1 line 1, page 22 line 26, page 26 line 21, page 29 line 2, page 36 lines 8 and 9, page 39 line 39 and page 56 line 27, which incorporates by reference another document, does not comply with Article 5 of the PCT. The description should be complete in and of itself. A person skilled in the art should be able to understand the patent specification without reference to any other document.

7. The description does not comply with Article 5 of the PCT. Documents referred to in the description of an application must be available to the public. Reference to the documents on page 1 line 2 must be deleted.

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of : Box No. V

Claims 20 and 21, which are directed to parameters measured for determining the quality of life in the methods of claims 18 and 19 and when such parameters are measured is not inventive to a person skilled in the art as such parameters were known in the art to said skilled person. As for claims 23-25, 27 and 28 which further define the composition used in claims 18 and 19, such features are disclosed in D1 or D2 and as such also do not comply with Article 33(3) of the PCT. No inventive step would be required for a skilled person to employ the composition of D1 or D2 in the methods of claims 18 or 19.

With respect to claim 26, claimed SEQ ID NO: 1 differs from the MUC-1 polypeptide used in D1 or D2 in that it does not contain two additional amino acids added at the C-terminal end, one being lipidated. However, no inventive step can be acknowledged for the use of a polypeptide of SEQ ID NO:1 since the present application fails to demonstrate that a liposome vaccine comprising the polypeptide of SEQ ID NO: 1 provides a selective advantage over the polypeptide employed in the vaccine of D1 or D2. The purpose of the lipidation appears to be the facilitation of the polypeptide into a liposomal formulation so that the MUC-1 lipopeptide can be presented on the surface of the liposome (see page 21 of the present application). As such, the amino acid to lipidate at the terminus of the peptide is one that is an option to a skilled person in the art and as such claim 26 does not comply with Article 33(3) of the PCT.

Claim 6 lacks inventive ingenuity in view of D2 and D5 and therefore it does not comply with Article 33(3) of the PCT. Paragraph 41 of D5 discloses interleukin-2 (IL-2) serves as a useful adjuvant in a BLP25 based liposome vaccine because of its immuno-stimulating properties. Therefore, a person skilled in the art would require no inventive step to include IL-2 in the vaccine composition of D2 to treat a NSCLC patient.

Claims 29 is directed to a method to treat cancer in a subject with a MUC-1 based liposomal formulation comprising SEQ ID No: 1 or SEQ ID NO: 2 (or immunologically active variants thereof) whereby the levels of circulating MUC-1 in the subject's serum dictates whether said subject should be treated. The closest prior art is D1 or D2 and D6. D1 or D6 disclose treatment of a cancer (NSCLC or prostate cancer) but is silent with respect to treating subjects that do not have high serum MUC-1 levels. D6 discloses various MUC-1 serum levels measured prior to immunotherapy in poor prognosis patients as having high MUC-1 levels versus good prognosis patients as having low MUC-1 serum levels for different cancer types. The cancer types examined include breast, ovarian, colorectal and pancreatic cancer.

No inventive ingenuity would be required by a person skilled in the art in view of D6 to determine the threshold MUC-1 serum level in subjects with NSCLC or prostate cancer for which MUC-1 treatment is potentially beneficial and apply the method of treatment disclosed in D1 or D2 to treat said subjects. Consistent with this view, page 5 of the present application states that it is well within the purview of the skilled person to determine threshold levels of circulating MUC-1 peptides in different groups of individuals. Therefore, claim 29 does not comply with Article 33(3) of the PCT in view of D1 or D2 and D6.

In terms of dependent claim 30, it differs from D6 in that the treatment in D6 does not involve a MUC-1 based vaccine. D1 or D2 employs the MUC-1 based vaccine of the present invention but does not treat the claimed cancers. As such, no inventive step would be required to treat patients with said claimed cancers with the vaccine of D1 or D2 with the knowledge that threshold levels of MUC-1 for several of the claimed cancers have been determined by D6. Common knowledge teaches that the claimed cancers are cancers in which MUC-1 is expressed (see page 39 of the present application). Therefore, no inventive step would be required by a skilled person in the art to treat other cancers that express MUC-1 using the treatment method of D1 or D2 and application therewith of the principles taught in D6. Therefore claim 30 does not comply with Article 33(3) of the PCT in view of D1 or D2 and D6. The present application fails to demonstrate that the MUC-1 based liposome formulation can be used as a successful treatment for said claimed cancers. Absent any data demonstrating an unexpected result, claim 30 is not inventive.

Industrial Applicability

Claims 1-30 appear to define subject matter that has industrial applicability under Article 33(4) of the PCT.